Commissioner for Patents

File No. 16051-9US CC/DBB

REMARKS

Claims 1-38 are pending in the application. Claims 3-32 are under examination. Claims 1, 2 and 33-38 are withdrawn.

Specification

Applicants wish to respectfully point out that paragraph [0001] on page 1 of the description was amended to update the status of all patent priority applications as requested by the Examiner.

Claim rejections - 35 U.S.C. § 112

Claims 3-32 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which is not described in the specification. The Examiner mentioned that the scope of claims 3-32 encompasses all possible randomer oligonucleotides that are more than 10 nucleotides in length. The possible variations are enormous to such randomer oligonucleotides longer than 10 or 40 nucleotides in the claimed pharmaceutical composition. The Examiner further mentioned that the specification has not disclosed randomer oligonucleotides longer than 10 or 40 nucleotides with phosphorothioate linkage and 2'-O-methyl modification to the ribose moiety. Consequently, the Examiner mentions that claims 3-32 are too broad since there is no indication of possession of all oligonucleotides that are more than 10 nucleotides long and with phosphorothioate linkage and 2'-O-methyl modification to the ribose moiety. In order to overcome this rejection, Applicants respectfully point out that it is stated in the Manual of Patent Examining Procedure that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates

that the patentee has invented species sufficient to constitute the genus" (Manual of Patent Examining Procedure 2163.05).

It is thus believed that the present description discloses a sufficient and/or representative number of species. For instance, in Example 8 in the description, it is disclosed that the oligonucleotide REP 2006 (40mer phosphorothioate-randomer) has an anti-DHBV activity. In addition, enclosed is a Declaration of Dr. Jean-Marc Juteau, one of the inventors, reporting *in vitro* results demonstrating the antiviral activity of oligonucleotides of the present invention against hepatitis B viruses (HBVs). Thus, in the declaration, it is disclosed that REP 2004 (20mer phosphorothioate -randomer) and REP 2031 (40mer phosphorothioate -polyC) have also an anti-DHBV activity. The present application and Declaration submitted herewith are disclosing efficacy of at least 3 different oligonucleotides of more than 10 nucleotides long and with phosphorothioate linkage. It is believed that a person skilled in the art would recognize that the present disclosure provides a representative number of species and that the Applicants were in possession of the claimed genus comprising at least 10 nucleotides in length with antiviral activity occurring principally by a non-sequence complementary mode of action. In view of the arguments presented hereinabove, reconsideration and withdrawal of Examiner's rejection are earnestly solicited.

Claims 3-32 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which is not described in the specification. The Examiner mentioned that claims 3-32 are drawn to a pharmaceutical composition comprising a library of randomer oligonucleotides that are at least 10 or 40 nucleotides in length for preventing and treating of HBV infection. The Examiner mentioned that the present invention encompasses *in vivo* therapy and that *in vitro* assays cannot duplicate the complex conditions of *in vivo* therapy and results in *in vitro* systems may not be reproducible in *in vivo* systems. In order to overcome this rejection, the Applicants wish to submit that it is believed that a person skilled in the art, in view of the teaching found in the present application, would acknowledge that there is sufficient and substantive disclosure in the present description to allow such person to use the oligonucleotides of the present invention in a pharmaceutical composition approved for use in humans against HBV. Applicants

wish to respectfully point out that in copending application No 10/661,403, *in vivo* results demonstrating efficacy of the oligonucleotides of the present invention to inhibit viral infection in eight (8) different *in vivo* models (Simian Immunodeficiency Virus model, Friend Leukemia Virus model, Influenza virus model, respiratory syncytial virus, Herpes virus-2 model, Cytomegalovirus model, Ebola virus model and Vaccinia virus model) were submitted. In addition, in copending application No 10/661,402, *in vivo* assays demonstrating the antiviral activity of the oligonucleotides claimed in the present application, covering different viruses, i.e. different viral families, different strains, RNA and DNA viruses were also submitted. More specifically, the antiviral activity of oligonucleotides claimed in the present application has been demonstrated in 28 different viruses from 13 families. Further, in copending application No 10/661,415, *in vivo* results obtained with a model of RSV viral infections (respiratory syncytial virus cotton rat model) were also submitted. Consequently, it is clear that the teaching contained in the present application combined with the common general knowledge is predicative of success for *in vivo* therapy since demonstration was provided in various *in vivo* models, regarding different families of viruses. Thus, it is believed that the efficacy of the oligonucleotides claimed in the present application to inhibit viral infection of various families of viruses is predicative of success for *in vivo* therapy following infection with HBV. In addition, it is stated in the Manual of Patent Examining Procedure that:

> If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will ***be sufficient to establish therapeutic or pharmacological utility*** for a compound, composition or process.
>
> Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders.

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In view of the efficacy of such pharmaceutical composition to treat *in vivo* models following viral infection with at least different viruses from 13 families, there is credibility in asserting utility for treating HBV infection in a human with the present invention. In addition, Applicants respectfully point out that the USPTO is not entitled to substitute itself to the FDA in order to evaluate the clinical relevance of the present invention. In view of the arguments presented hereinabove, reconsideration and withdrawal of Examiner's rejection are earnestly solicited.

Double Patenting

Claims 3-32 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 and 18-26 of copending Application No. 10/661,403. In addition claims 3-32 have also been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-51 of copending Application No. 10/661,402, over claims 3-32 of copending Application No. 10/661,415, and over claims 23-52 of copending Application No. 10/969,812. . In order to overcome these rejections, Applicants respectfully request the Examiner to hold the requirement for submission of a terminal disclaimer in abeyance until such time as either application is found to be in otherwise allowable condition.

It is submitted, therefore, that the claims are in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested. Allowance of claims 3-32 at an early date is solicited.

No additional fees are believed to be necessitated by this amendment. Should this be in error, authorization is hereby given to charge Deposit Account No. 19-5113 for any underpayment or to credit any overpayment.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

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Respectfully,

Date: November 2, 2006

By: _____

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Enc.: Declaration
CV of Dr. Juteau
Petition for extension of time

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Christian Cawthorn
Name of person signing certification

_____ November 2, 2006
Signature Date